Interests Intersect: Technology and Training Combine to Find Answers

JAMES WOHLSCHLEGEL came to science at a time when his two interests could intersect - the global analysis of proteins with mass spectrometry and using his biological chemistry training to study cell signaling pathways that are mis-regulated in cancer.

He was definitely at the right place at the right technological time.

Wohlschlegel, an assistant professor of biological chemistry who joined the UCLA faculty in the fall of 2006, always wanted to be a scientist. He liked figuring out how things worked.

Near the end of high school, he entered a project in the science fair and loved the time he spent preparing it in a laboratory.

"Being a scientist is a career where you're given the freedom and independence to ask questions that are interesting to you, how some fundamental life process works," said Wohlschlegel, 34, who was born in Taiwan to an American father and a Japanese mother. "You get to ask the questions in a number of ways and be creative about how to get your answers." (Click here to see Wohlschlegel talk about his desire to be a scientist.)

Wohlschlegel attended Texas A&M University and worked in a laboratory from his first day, studying bacterial genetics. It was his first exposure, he said, to "cutting-



edge, mainstream experimental science."

He was hooked.

Wohlschlegel worked in the bacterial genetics lab for two years before moving to a lab that focused on enzyme reaction mechanisms, providing him with his first exposure to biological chemistry. He promptly made biological chemistry his major.

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After graduation, Wohlschlegel attended Harvard Medical School where he pursued a doctorate in biological chemistry. There, he joined a lab that studied cell cycle control and DNA replication in cancer. This exposure to cancer cell biology again altered his scientific path, just as his later experiments would take him down different pathways in his quest to uncover what could be a cause of cancer.

After earning his doctorate from Harvard, Wohlschlegel went to the Scripps Research Institute in La Jolla in 2002 with a very specific goal – to work in the lab of analytical chemist John Yates, who was developing methods for global analysis of proteins using mass spectrometry, an analytical technique that is able to determine the identity of proteins based on their weight. He also worked in the lab of Steve Reed, who specialized in the regulatory mechanisms of cell cycle control.

In the Yates lab Wohlschlegel could develop new methods or techniques to study the biological processes he was focusing on in Reed's lab. And so his interests – and technology – intersected.

Specifically, Wohlschlegel wanted to study the ubiquitin family of small modifier proteins, which get attached to target proteins in the cell and regulate their activity. For the next four years, Wohlschlegel developed various proteomic methods and techniques that enabled him to study the biological importance of ubiquitin and SUMO, a ubiquitin family member, at a global level to see how these different proteins are organized into large regulatory networks that are

JAMES WOHLSCHLEGEL

central to their function. (Click here to see Wohlschlegel talk about his work.)

Ready to launch his own lab, Wohlschlegel sought a place to call his scientific home. UCLA was attractive to him because many scientists were doing work that was complementary to his and also because of the highly collaborative atmosphere that is fostered at the university and within UCLA's Jonsson Comprehensive Cancer Center.

And because UCLA was a large academic institution, he would have his own mass spectrometer and the flexibility to pick and choose his collaborations to best bolster his own research.

Again his interests have merged. He is back where he started, focusing on biological chemistry, but using mass spectrometry to study the proteins at work in cells and how they regulate their growth and development.

He is still focusing on the ubiquitin family of small protein modifiers and hoping, through his work, to characterize the functions of a huge number of enzymes that are responsible for attaching ubiquitin to target proteins,

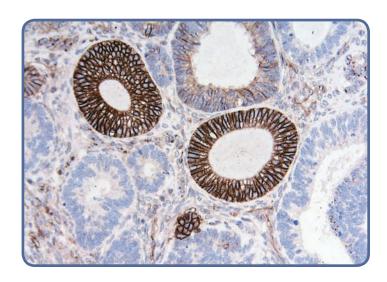
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but whose biological purposes have remained a mystery. Between 500 and 700 enzymes remain uncharacterized, Wohlschlegel said, and if their function can be revealed it may answer some fundamental questions about the development of certain cancers.

"This is a very open area of biology," Wohlschlegel said. "We know these enzymes are important and it's a great opportunity with the technology we have now to study them and get some quick answers. We know some of these enzymes are de-regulated in cancer."

Wohlschlegel currently is focusing on a subset of enzymes he thinks may have a role in the development of cancer. He doesn't know where that road will lead him scientifically, but, for him, that's really not the point.



"It almost doesn't matter to me where (the investigation) goes," he said. "It's going to be interesting whatever happens. It's an exciting time in that with the technology we have we can ask really sophisticated questions about a biological system. Our tool set really enables us to approach problems at different levels from the reductionist analysis of individual components to system-level analyses that help us to see how these components fit together."

"I feel like I'm at the interface of two fields, mass spectrometry and traditional molecular biology and there's where I'm trying to carve a niche for myself," he said. "I can integrate the two fields and ask questions that are uniquely mine."